

groups was 5 mg. 35/54 AM patients (64.8%) developed stomatitis of any grade (CTCAE grade 1 27.8%; grade 2 20.4%; grade 3 11.1%) compared with 13/23 AM+S patients (56.5%) (CTCAE grade 1 30.4%; grade 2 17.4%; grade 3 8.6%); $P = 0.49$. There was no difference between the frequency of grade 2–3 stomatitis between the AM group (31.5%) and the AM+S group (26.1%); $P = 0.67$. Stomatitis was an early toxicity in both groups, occurring during cycle 1 in almost 70% of patients in the AM group and the AM+S group. Everolimus was discontinued due to stomatitis in 12% of patients in both groups.

Conclusion: The addition of a betamethasone mouthwash did not reduce the rate of everolimus-related stomatitis. The rate of grade 2–3 stomatitis was significantly higher in our study (26.1%) than reported in the SWISH clinical trial with the dexamethasone mouthwash (2%). This audit highlights the significant challenges that still exist with administering everolimus in the real-life clinical setting.

References

- [1] Baselga J, Campone M, Piccart M, Burris HA, Rugo HS, Sahnoud T et al. Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer. *New Engl J Med* 2012;366:520–9.
- [2] Rugo HS, Seneviratne L, Beck JT, Glaspy JA, Peguero JA, Pluard TJ et al. Prevention of everolimus-related stomatitis in women with hormone receptor positive, HER2 negative metastatic breast cancer using dexamethasone mouthwash (SWISH): a single arm, phase-2 trial. *Lancet Oncol* 2017;18:654–62.

A Real-world Analysis of the Treatment of HER2+ Metastatic Breast Cancer (mBC) Beyond First-line HER2-directed Therapies

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Purpose: The treatment of HER2+ mBC is clinically challenging and treatment algorithms continue to be updated based on clinical trial outcomes. Challenges to treatment sequencing include prior exposure to HER2-directed therapies, including exposure in the neoadjuvant/adjuvant setting. We interrogated our Sussex Cancer Network mBC dataset to determine real-world patterns in HER2+ disease responses.

Methods: Clinical coding was used to identify patients treated by the breast oncology team for HER2+ mBC between 2014 and 2017. Clinical notes, radiology and chemotherapy e-prescribing records were used to collect histopathological, treatment and survival data.

Results: In total, 86 patients were treated for HER2+ mBC, of which 34.8% ($n = 30$) presented with *de novo* HER2+ mBC. In the first-line setting, 79% of patients ($n = 68$) received HER2-directed therapies, of which 51% ($n = 35$) received docetaxel/trastuzumab/pertuzumab, 38% ($n = 26$) received other cytotoxic agents, i.e. paclitaxel, capecitabine, vinorelbine, and the remaining 11% ($n = 8$) received endocrine treatment in combination with HER2-targeted therapies. Patients received a median of 2.5 lines (1–8) of treatment. Sixty per cent ($n = 52$) received second-line therapies on progression, of which chemotherapy in combination with HER2-directed therapies (57.6%, $n = 30$) and endocrine-only (21%, $n = 11$) were the most commonly used treatment modalities. The median overall survival for this HER2+ patient group was 34 months. Survival analysis indicates that continuity of systemic therapy correlates with median overall survival, i.e. one line (15.5 months, $n = 31$), two to three lines (26.7 months, $n = 33$) and more than three lines (38.8 months, $n = 20$). Interestingly, a difference in median overall survival was observed between patients with *de novo* mBC (44.4 months, $n = 30$) when compared with patients previously treated for early breast cancer (19.5 months, $n = 56$), suggesting that disease recurrences following exposure to trastuzumab may be associated with poorer outcomes influenced by alternate pathways of resistance.

Conclusion: This analysis indicates that continuing beyond three lines of treatment may be beneficial to overall survival, while contributing to the argument that treatment plans for HER2+ mBC need to be individualised, factoring in the timeline of previous exposure to HER2-targeted therapies. Predictive biomarkers could play a role in predetermining resistance/response and aid in rationalising treatment plans. Our onward analysis will

assess the influence of the hormone receptor status in the treatment responses of HER2+ mBC.

Prospective Observational Study in Patients with Metastatic Breast Cancer Involving the Central Nervous System (PRIMROSE)

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Purpose: Central nervous system (CNS) involvement from breast cancer is an increasing clinical problem and is associated with a poor prognosis. Incidence of CNS metastasis and response to treatment varies by breast cancer subtype and no breast cancer-specific CNS metastasis guidelines currently exist to help guide management. Treatment options include surgery, stereotactic and whole brain radiotherapy, systemic and intrathecal therapies. There is a need to understand how current treatment paradigms affect CNS metastasis outcomes across subtypes, and generate data to inform future practice guidelines.

Methods: This prospective, multicentre observational study aims to register patients diagnosed with CNS involvement secondary to breast cancer throughout the UK and will collect data relating to the primary breast cancer and extracranial metastatic disease, presentation and diagnosis of CNS metastasis and CNS-directed treatment outcomes. The primary outcome is measurement of overall survival from the time of diagnosis of CNS metastasis. Secondary outcomes include prevalence of brain metastasis by subtype and progression-free survival (local/brain relapse versus relapse at other sites) following therapy. Inclusion criteria are female or male patients with breast cancer of any subtype, with histologically or radiologically confirmed breast cancer involving the CNS or diagnosis of a paraneoplastic syndrome. This is a trainee-led study involving specialist registrars training in medical oncology, clinical oncology, pathology and neurosurgery. Study sites cover major cancer centres and peripheral centres throughout the UK. The study will be registered at individual sites according to local trust policy. Subjects will be identified via breast cancer clinical teams, acute oncology services, neurologists, neurosurgical multidisciplinary teams and radiotherapy referrals. Data will be recorded and stored on a centralised data system, RedCap, in compliance with ICH-GCP. Data collection will start early 2019 and the first database lock for evaluation of number and data spread will be carried out after 8 months.

Results: N/A (study in progress).

Conclusion: N/A (study in progress).

Role of Primary Chemotherapy in Women with Biopsy-proven Lymph Node-positive Breast Cancer

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Purpose: Women with lymph node-positive early breast cancer who achieve a good response to primary chemotherapy could potentially avoid axillary node clearance (ANC) and proceed to sentinel lymph node biopsy (SLNB) [1]. This would reduce the risk of significant lymphoedema. We have previously reported response rates in the axilla following primary chemotherapy in our population [2]. We now report on 30 patients who had a marker clip inserted in the lymph node prior to primary chemotherapy. At the time of breast surgery, patients either underwent ANC or SLNB with at least three lymph nodes removed, including the marker clip, to enable accurate assessment of response.

Methods: This was a retrospective single-centre study. We examined the records of all patients, through the Guy's Breast Cancer Database and chemotherapy prescribing system, who had node-positive breast cancer, marker clip in the axilla and primary chemotherapy from October 2016 to October 2017.

Results: We identified 30 patients with lymph node-positive disease, who had primary chemotherapy. At the time of surgery, 7/30 had a pathological complete response (pCR) in the axillary lymph node. Of these, 5/7 patients

had pCR in the axillary lymph node and primary breast tumour and 2/7 had pCR in the axillary lymph node with a partial response in the primary breast tumour. Five patients had residual disease in the axillary lymph node and a pCR in the primary breast tumour. All axillary clips were successfully retrieved at surgery.

Conclusion: 35.7% of patients who had primary chemotherapy achieved pCR in the axilla (30% in the published data) [1,2]. 23.3% with a marker clip had SLNB at the time of surgery. Our results suggest that not all patients with lymph node-positive disease need ANC if they respond well to chemotherapy. More work is needed to establish if we can accurately recognise which patients can be managed with SLNB.

References

[1] Boileau JF, Poirier B, Basik M, Holloway CM, Gaboury L, Sideris L et al. Sentinel node biopsy after neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: the SN FNAC study. *J Clin Oncol* 2015;33:258–64.

[2] Germanou S, Chowdhury MHR. Could women with biopsy proven lymph node positive breast cancer and response to primary chemotherapy avoid axillary lymph node clearance? *Clin Oncol* 2018;30:e43–4.

A Closed-loop Audit of 5 versus 10 Days of Primary GCSF Prophylaxis to Reduce the Incidence of Febrile Neutropenia in Early Breast Cancer Treatment

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Purpose: Current guidelines recommend that patients with early breast cancer receiving chemotherapy that confers >20% risk of febrile neutropenia should have primary prophylactic granulocyte colony-stimulating factor (GCSF) on days 2–6 of chemotherapy [1,2]. An initial audit [3] demonstrated non-inferiority of 5 days versus 10 days of primary prophylactic GCSF in respect of febrile neutropenia rates seen in early breast cancer chemotherapy. Since 1 August 2016, our centre has switched from 10 days of prophylactic GCSF to 5 days. We re-audited febrile neutropenia rates following our change in practice.

Methods: The initially audited patient cohort received chemotherapy between August 2016 and February 2017. We closed the audit loop by analysing data for all patients at our centre receiving chemotherapy for early breast cancer between April 2017 and March 2018. Patient and treatment details were taken from ChemoCare® and blood results from Medway®.

Results: We identified 49 patients. The rates of febrile neutropenia were 24% in the 5-day GCSF cohort compared with 7.4% in the 10-day cohort. Eighty-five per cent of the admissions with febrile neutropenia occurred after the 5-day course of prophylactic GCSF was completed. The median length of stay was 2.5 days. Four patients (33%) had their prophylactic GCSF extended following febrile neutropenia. Eight patients (66%) had their chemotherapy dose reduced and one patient had their chemotherapy stopped following admission. The cost–benefit analysis, per patient, for 10 days GCSF is £540.29 and for 5 days GCSF is £383.95¹.

Conclusion: The previously demonstrated non-inferiority of 5 days versus 10 days of prophylactic GCSF in relation to febrile neutropenia rates was not corroborated in our re-audit. This may be partly attributable to a variation in patient characteristics between the two cohorts. Additionally, although a cost–benefit analysis favours the 5-day regimen, this does not account for morbidity related to GCSF or neutropenia. Patients of increased body weight should receive a higher dose of GCSF.

¹Cost–benefit analysis: GCSF cost + (chance of febrile neutropenia × cost per bed day × median length of stay). For 10 days GCSF: (250.75 × 2) + (0.07 × 222 × 2.5) = £540.29. For 5 days GCSF: (250.75 × 1) + (0.24 × 222 × 2.5) = £383.95.

References

[1] Smith TJ, Bohlke K, Lyman GH, Carson KR, Crawford J, Cross SJ et al. Recommendations for the use of WBC growth factors: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 2015;33(28):3199–212.

[2] London Cancer: Systemic treatment for breast cancer. Version 1.1 (January 2014 update). Available at: <http://www.londoncancer.org/media/72921/>

london_cancer_breast_systemic_guidelines-v1.1-january-2014-update.pdf.

Accessed 17 August 2018.

[3] Smith T, Jenkinson S, Raja F. A study into GCSF primary prophylaxis for early breast cancer chemotherapy: a comparative study from two cancer centres in North London. *Clin Oncol* 2017;29(6):e103.

Partial Breast Radiotherapy: a Single Centre Experience

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Purpose: This audit was undertaken to assess if the recurrence rates following partial breast radiotherapy at the Christie were in keeping with the IMPORT LOW trial [1], which showed non-inferiority when compared with whole breast radiotherapy for local recurrence. We also evaluated our selection criteria for partial breast radiotherapy with inclusion criteria used in the IMPORT LOW trial [1].

Methods: A retrospective analysis between April 2010 and April 2013 was undertaken using clinical records and local PACs systems. All patients reached 5 years post-treatment. Local protocol for follow-up is annual mammographic surveillance.

Results: In total, 63 patients were treated with partial breast radiotherapy, with one having bilateral treatment. The median age was 62 years. Twenty patients were aged 50–59, 43 aged >60 years and one <50 years (46 years). Fifty-six patients had invasive ductal carcinoma; the majority had grade 1 (42%) or grade 2 disease (44%). Sixty patients (95%) had hormone-positive disease. Fifty-four had standard hypofractionated radiotherapy (40 Gy in 15 fractions). Seven had a lower total dose (37.5 Gy and 38.5 Gy). One patient received 37.5 Gy in 14 fractions. All patients completed the intended treatment course.

Sixty of 63 were alive at the time of the retrospective review. Three died from metastatic disease from an unrelated second primary. Of those 59 patients who completed 5 years of mammographic follow-up there was no evidence of local recurrence (100%). Of the four patients who did not have 5 years of mammography, two were lost to follow-up, one died of a second primary and one had 4 years of mammography follow-up but no final mammogram. Adherence to the patient inclusion criterion set in the IMPORT LOW trial was good (98–100%).

Conclusion: The rate of local recurrence following partial breast radiotherapy is low when appropriately used in the low-risk patient and should be considered in this cohort routinely.

Reference

[1] Coles CE, Griffin CL, Kirby AM, Titley J, Agrawal RK, Alhasso A et al. Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial. *Lancet* 2017;390(10099):1048–60.

Clinical Outcomes in HER2-positive Lobular Breast Cancer: a Single-institution Experience

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Purpose: Invasive lobular carcinomas (ILC), characterised by loss of the cell adhesion molecule E-cadherin, are typically oestrogen receptor (ER)-positive/HER2-negative luminal tumours with a similar prognosis to that expected for luminal invasive ductal carcinomas (IDC). Less than 5% of classical ILC but up to 35% of pleomorphic ILC are HER2-positive. Previous studies have suggested similar benefit from trastuzumab for HER2-positive ILC and IDC, but data are limited [1].

Methods: Retrospective collection of clinical data from all patients with HER2-positive ILC diagnosed between 2004 and 2014 at the Royal Marsden Hospital. The primary end point was median overall survival in patients with metastatic HER2-positive ILC, secondary end points included timing and pattern of relapse after treatment for early HER2-positive ILC and rate of pathological complete response (pCR) to neoadjuvant chemotherapy (NAC).